

## POSTER SESSION 2

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**P414****Cardiac pacing modifies connexin43 localization within the intercalated disc during ischaemia, 24h later**

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**Purpose:** We have now examined whether the ischaemia-induced structural alterations of the main gap junction (GJ) protein connexin43 (Cx43) are modified by rapid cardiac pacing, 24h previously.

**Methods:** Under light pentobarbital anesthesia, in 8 dogs a pacing electrode was introduced into the right ventricle through which, in half of these dogs, the heart was paced four times for 5 min at a rate of 240 beats/min. Twenty-four hours later, both the non-paced controls (SPO; n=4) and the paced (PO; n=4) animals were subjected to a 30 min occlusion of the left anterior descending (LAD) coronary artery. Another 3 dogs were also instrumented, but these animals were not subjected to either pacing or coronary artery occlusion (SP, n=3). In each experimental group left ventricular tissue samples from the LAD region were taken for immunohistochemical, western blot and co-immunoprecipitation analyses.

**Results:** The immunohistochemical images showed that a 30 min of ischaemia resulted in increased intensity of Cx43 and obvious structural alterations of the intercalated discs (ID); the connections became disoriented and 'blurred' particularly at the longitudinal sections. In contrast, in the paced dogs the structural integrity of GJs was well-preserved and the intensity of Cx43 was reduced to the same level as has been observed in the SP group. Under normal conditions, the GJs are mainly located at the periphery of the ID, the intensity and size of GJs is less pronounced at the center region of the disc. Ischaemia altered this distribution pattern resulting in enhanced intensity in both the peripheral and central regions of the ID. These ischaemia-induced changes were, however, almost completely abolished by pacing, commenced 24h previously. Compared with the SP dogs, ischaemia reduced the phosphorylation and increased the dephosphorylation of Cx43 (phospho/dephospho ratio was 40/60%). Pacing reversed this phospho/dephospho ratio of Cx43 (55/45%).

**Conclusions:** These results suggest that rapid cardiac pacing favorably modifies the ischaemia-induced structural changes of GJs occurring within the ID. The preliminary results of the co-immunoprecipitation studies indicate that these changes may associate with alterations in the connection of Cx43 and ZO1 proteins.